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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/274,752 | 03/23/1999 | EDWARD J. GOETZL | A-67501/DJB/ | 8855 |

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| EXAMINER |
|---|
| HARRIS, ALANA M |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1642 | 33 |

DATE MAILED: 09/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/274,752 | GOETZL ET AL. | |
| | Examiner | Art Unit | |
| | Alana M. Harris, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with th correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1,3,4,6-11 and 21-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *21-31* is/are allowed.

6)☒ Claim(s) *1,3,4 and 6-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *28,29* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Response to Arguments*

1. Claims 1, 3, 4, 6-11 and 21-31 are pending.

Claims 2, 5 and 12-20 have been cancelled.

Claims 1, 3, 4, 21 and 27-30 have been amended.

Claims 1, 3, 4, 6-11 and 21-31 are examined on the merits.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### *Withdrawn Objections*

### *Specification*

3. The disclosure is no longer objected to because it has been amended to no longer contain an embedded hyperlink and/or other form of browser-executable code on page 6, line 10.

### *Claim Objections*

4. Claims 21 and 27 are no longer objected to under 37 CFR 1.75 as being a substantial duplicate of one another because these claims have been amended.

***Withdrawn Rejections***

***Claim Rejections - 35 USC § 112***

5. The rejection of claims 1, 3, 4 and 6-11 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is withdrawn. Claims 2 and 5 have been cancelled.

6. The rejection of claims 21-31 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention is withdrawn in light of the claim amendments.

7. The rejection of claim 24 under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials is withdrawn in light of the ATCC deposit information.

8. The rejection of claims 3 and 4 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention is withdrawn due to claim amendments. Claim 5 has been cancelled.

***Claim Rejections - 35 USC § 102***

9. The rejection of claims 1, 3, 4 and 6-11 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 6,020,158 (filed May 22, 1997) is withdrawn. Claims 2 and 5 have been cancelled.

10. The rejection of claims 1, 3 and 6-11 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent number 5,856,443 (filed December 6, 1996) is withdrawn. Claim 5 has been cancelled.

11. The rejection of claims 1, 3 and 6-9 under 35 U.S.C. 102(b) as being anticipated by GenBank Accession number AA419064, clone 755526 (May 12, 1997/ IDS Reference 2, Paper 13) is withdrawn in light of Applicants' arguments. Claim 5 has been cancelled.

12. The rejection of claims 1, 3 and 4 under 35 U.S.C. 102(b) as being anticipated by MacLennan et al. (Molecular and Cellular Neurosciences 5:201-206, 1994) is maintained. Claims 2 and 5 have been cancelled.

13. The rejection of claims 1, 3 and 6-11 under 35 U.S.C. 102(a) as being anticipated by An et al. (April 3, 1998/ IDS Reference 3, Paper 6) is withdrawn. Claims 2 and 5 have been cancelled.

***Maintained Grounds of Rejection***

***Claim Rejections - 35 USC § 112***

14. Claims 1, 3, 4 and 6-11 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 2 and 5 have been cancelled.

Applicants point out that the language of record in the first action on the merits, page 5, paragraph 10 presents language consistent with a written description rejection, however there is a lack of enablement rejection. The Examiner concurs with Applicants and duly notes the error. The instant rejection is consistent with a lack of written description.

Applicants have amended the claims to now recite " at least 95% sequence identity" and argue that the specification ...as filed clearly allows persons ...to recognize that applicants were in the possession of the invention...". Applicants further aver that the inventor is not obligated to describe every single detail of his invention and Edg4

and Edg5 show a significant degree of homology with other members of the family. These points of view have been carefully considered but found unpersuasive.

The Examiner has reviewed Applicants' disclosure and with particularity the pages listed by Applicants, which address significant shared sequence homology with the Edg family of receptors. Applicants' disclosure does not set forth any nucleic acid sequences other that SEQ ID NO: 2 and 4 that encode amino acids, SEQ ID NO: 1 and 3, respectively. The claims embrace nucleic acids other that SEQ ID NO: 2 and 4 that encode amino acids that have at least 95% sequence identity to SEQ ID NO: 1 and 3. Applicants have not provided sufficient evidence or guidance that they were in possession of the claimed molecules, or established the modifications in which one or more nucleic acid residues have been inserted, deleted or replaced. Consequently, has not been clearly established that the encoded modified amino acid sequence will retain the biological activity of the Edg proteins. Remiss from the disclosure is evidence that Applicant was in possession of a representative number of species encompassed by the broad genus. The variations, in which Applicant's disclosure suggests are substantial, see pages 9 and 10. Applicants have not provided structural and functional activity of the variant Edg molecules encompassed by the claims. There is insufficient evidence of record suggestive that Applicant was in possession of variant polypeptides with the structural and functional characterization necessary for retaining receptor activity for lysophospholipids and sphingolipids.

As set forth in the Official Gazette issued January 30, 2001, page 1242 OG 174, column 1, section 2 the written description requirement for a claimed genus may be

satisfied through sufficient description of a representative number of species by actual reduction to practice, wherein one must describe a sufficient variety of species to reflect the variation within the genus where there is substantial variation with the genus as Applicant's claims propose. Additionally, "adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus". There is insufficient to support the generic claims as provided by the Interim Written Description Guidelines published in the June 15, 1998 Federal Register at Volume 63, Number 114, pages 32639-32645.

The full breadth of the claims does not meet the written description provision of 35 U.S.C. 112, first paragraph.

15. The rejection of claims 1, 3 and 6-11 under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement commensurate with the scope of the claimed invention is maintained.

Applicants argue that the "[a]though the Examiner acknowledges that the specification teaches modification within the native Edg4/5 sequences, she maintains that there is no evidence which modifications yield polypeptides that maintain the activities proposed...". Furthermore, Applicants aver "the present Edg4/5 proteins have been identified as members of the family of Edg receptors" and consequently presume that the broadly claimed molecules would maintain the functions of the native protein. These arguments have been considered but found unpersuasive.

The information regarding the modifications which can be made within Edg4/5 sequences is plainly prophetic. And while the Examiner acquiesces that more than likely these changes can be made, there is insufficient disclosure supporting the implementation of the suggested modifications within Edg4/5 molecules. Likewise, there is not indication that the resulting molecules are capable of acting in the same manner as the wild type protein. Activity based on sequence homology is not a full-proof test of biological activity. As set forth by Smith et al. (1997, Nature Biotechnology 15:1222-1223) there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. It follows that without sufficient guidance, the changes which must be made in the nucleic acid sequences, SEQ ID NO: 2 and 4 and amino acid residues of SEQ ID NO: 1 and 3, which results in less than 100% sequence identity is unpredictable and the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

***Claim Rejections - 35 USC § 101***

16. The rejection of claims 1, 3, 4 and 6-11 under 35 U.S.C. 101 because the claimed invention is not supported by either a specific, credible or substantial asserted utility or a well established utility is maintained. Claims 2 and 5 have been cancelled.

Applicants argue that they "...have established a substantial, specific and credible utility for the Edg4 and Edg5 proteins of SEQ ID NOS: 1 and 3, respectively" and "it is clear for those skilled in the art at the filing date...that the native proteins.. of

the present t application can be altered, without losing their biological activity". These arguments have been considered but found unpersuasive.

Applicants' specification does not provide data that supports utility of variant proteins implicated to be effective in applications germane to the invention, for example as a tool to determine the effectiveness of a candidate bioactive agent (see page 8, lines 22-25) and "...in the study or treatment of conditions related to phospholipid mediators LPA and S1P" (see page 40, lines 12-14). It is clear that even the wild type Edg proteins' activity of the present invention is speculative, see page 39, line 22-25. This questionability is provides impetus for one skilled in the art to reasonably doubt the variant proteins' utility. Given the lack of evidence the utility is not yet known and has not yet been disclosed and not substantial because it not currently available. Accordingly the claimed isolated polynucleotides and polypeptides lack credible, substantial or specific utility.

Claims 1, 3, 4 and 6-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific, credible or substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. Even if Applicants were to evidence that claims 1, 3, 4 and 6-11 have a patentable utility they would not be enabled for the full scope of the invention.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alana M. Harris, Ph.D. whose telephone number is

(703) 306-5880. The examiner can normally be reached on 7:00 am to 4:30 pm, with alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached on (703) 308-3995. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

ALANA HARRIS
PATENT EXAMINER

Alana M. Harris, Ph.D.
September 11, 2003